UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/986,568	12/05/1997	JEAN-FRANCOIS BACH	040388/0110	5102

7590 11/12/2003

STEPHEN A BENT
FOLEY & LARDNER
3000 K STREET NW SUITE 500
PO BOX 25696
WASHINGTON, DC 200078696

EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 11/12/2003

36

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 36

Application Number: 08/986,568
Filing Date: December 05, 1997
Appellant(s): BACH ET AL.

Stephen A. Bent
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed December 10, 2002.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences, which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

Specifically, there are none.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

Appellant's brief presents arguments relating to the issue of whether the examiner properly reopened prosecution of the instant case following a Broad decision. This issue relates to petitionable subject matter under 37 CFR 1.181 and not to appealable subject matter. See MPEP § 1002 and § 1201.

Appellant submitted such a petition in Paper 30. This petition was dismissed and denied (Paper 32).

(7) Grouping of Claims

Appellant considers the claims to stand or fall together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

Journal	Name	Date
Proc. Natl. Acad. Sci. U.S.A.	Chatenoud et al.	1994

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims: Claims 1, 6, 9-13 and 17-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Appellant did not posses the genus of "anti-CD3 active compounds".

The only examples of such compounds that appellant has given or suggested are antibodies to CD3 (or compounds that would also be encompassed by antibodies, such as antibody fragments, humanized antibodies, etc.) Appellant has directed the reader to no other genre of compounds, nor could one readily envision other kinds of compounds such as lipids, carbohydrates, or non-Immunoglobulin polypeptides that would be "anti-CD3 active". Appellant has disclosed no other type of compound which, like an anti-CD3 antibody, is capable of binding to CD3 in a ligand-receptor manner Appellant has merely described the genus by functional language has failed to describe any type of common structure that such a genus of compounds must have in order to bind to the CD3 antigen. Appellant has thus failed to adequately describe the genus of "anti-CD3 active" members, except for those members which are anti-CD3 antibodies.

Claims 1-2, 4-7, 9-13 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Appellant has not enabled the treatment of established autoimmune disease in humans.

Appellant's disclosure has only exemplified NOD strain mice, and it would be unpredictable as to whether or not such treatments would also be efficacious in humans. Appellant and co-authors have clearly admitted that the same results obtained in NOD mice (as shown in the 103(b) reference of Chatenoud et al.) would need to be "confirmed" in humans and that such a therapy is only a "possibility". See page 127, col. 2, last full para.

Appellant's disclosure has shown nothing, beyond what is disclosed or readily extrapolated from Chatenoud et al., to further develop the invention for human treatment. Specification page 4 merely gives general statements regarding administration of the compound along with pharmaceutical carriers and regarding routes of administration. These statements merely recite what those of skill, or even those having peripheral acquaintance, in the art would have already known regarding treatment with proteinacious pharmaceuticals. The only specific information given at page 4, with respect to treating humans, is that regarding the dosage range. However, this range merely encompasses the dosage taught by Chatenoud et al. for mice when that dosage is extrapolated to

humans on a body weight basis (see 103 rejection regarding claims 17-18, infra, for calculation).

Examiner thus fails to see what new information this disclosure provides that is particularly relevant to treating humans.

Claims 1-2. 4-6, 9-13 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chatenoud et al. (PNAS, 91, 123-127 (1994).

Chatenoud et al. teach treatment of NOD mice having an overt/established autoimmune disease (diabetes) via injection with a purified, endotoxin-free, monoclonal anti-CD3 F(ab')2 fragment.

The particular anti-CD3 F(ab')2 fragment used by Chatenoud et al. (page 123 col. 2) is precisely the same as that exemplified by appellant (specification page 5). As an F(ab')2 fragment, this antibody is taken to be inherently non-mitogenic (see specification page 1, lines 32-33; page 2, lines 23-28; page 3, lines 11-21). It is thus considered that the antibody fragment of Chatenoud et al. had the "non-nitogenic" limitation of claims 1-6 and the "endotoxin-free" limitation of claim 6.

Chatenoud et al. teach that these treatments provide long term remission of the autoimmune disease. See title; see abstract at lines 9-14; see paragraph spanning pages 125-126, and paragraph spanning pages 126-127; see page 127, col. 1, second full paragraph.

Chatenoud et al. thus teach all aspects of instant claims 1-2, 4-6, 9, 13 and 16, except for the fact that they treat mice instead of humans. However,

they clearly teach that it would be desirable to extend this treatment to humans (page 127, col. 2). It thus would have been obvious to treat human diabetes with non-mitogenic anti-CD3 fragments as taught by Chatenoud et al.

Regarding claims 10-12, which recite well known autoimmune diseases other than diabetes, the treatment of any of these would have been obvious because the anti-CD3 antibody of Chatenoud et al. modulates the CD3/TCR cell surface receptor complex, irrespective of the antigenic specificity of the TCR. Hence one would have expected that modulation of the CD3/TCR complex, by administration of anti-CD3, would likewise be efficacious in treating any established autoimmune disease in which the TCR recognizes an autoantigen other than that involved in diabetes.

Regarding claims 17-18, it is noted that Chatenoud et al. used doses of 5ug/day for mice. Taking the typical weight of a human to be 70kg and the typical weight of a mouse to be 20g (.02kg), one of ordinary skill would have expected that multiplying the dose given to mice by a factor of 70/.02 (or 3500) would provide a dose appropriate for humans. That is, 5ug/day X 3,500 gives a dose of 17.5mg/day for humans. This clearly falls within the range recited in claim 17, and it falls within a factor of 2 of the range recited in claim 18, which factor is considered good enough for stating obviousness in biological systems which do not typically operate within only a narrow range of parameters.

The examiner briefly notes that claim 7 is not included in the statement of the rejection set forth supra, as in the Final rejection (Paper 33, page 3).

Whether this was left out by oversight or not, the examiner cannot recall. However, the claim recites nothing more than a conventional source of monoclonal antibodies "murine" (this term is broader than mouse; it is not encompass hamster antibodies used by Chatenoud et al.), and "humanized" (desirable for treating humans). In any event appellant considers that all claims stand or fall together (Grouping of claims, at page 2 of Brief). Thus no formal rejection of claim 7 is required.

(11) Response to Argument

Appellant has argued (Brief pages 3-5) that the examiner improperly reopened prosecution after a decision by the Board. As the examiner has noted supra, this is an issue for petition, not for appeal. No further comment is necessary.

With respect to arguments concerning the 112, first paragraph, lack of possession rejection, appellant has taken the position that "all anti-CD3 active compounds" would take the form an "immunoglobulin or a fragment" thereof" (Brief, page 6, lines 2-3). Curiously, this position agrees with the examiner's statement of the rejection –i.e. that one of skill could not readily envision the structural features of any members of the genus, other than antibodies/immunoglobulins or fragments thereof. The examiner thus finds no argument to which he should respond. In any event, the above noted statement by appellant has estoppeled against any broader interpretation of the term "anti-CD3 active compounds" beyond antibodies/immunoglobulins and fragments

thereof, despite the fact that the specification has placed no such limitation upon the term.

With respect to arguments regarding the 112 enablement rejection, applicant has urged that proof of human efficacy, by exemplification, is not necessary and that the NOD mouse is an art accepted model (appellant attached various references that use NOD mice as models for various therapies pertaining to diabetes; not all of these treat with compounds within the scope of the instant claims). The examiner notes that while these references generally acknowledge that NOD mice are a model for human diabetes, they do note some differences in the features of diabetes in NOD mice and humans (e.g. Bowman et al. page 115, paragraph spanning columns 1-2). The examiner does not have the technical expertise to determine whether or not these differences would be crucial to predictability of results using the instant compounds.

What is more crucial than whether or not the NOD mouse model is appropriate is that appellants and co-authors have admitted in the Chatenoud et al. reference, cited under 103, that the results obtained with mice would need to be "confirmed" with humans (page 127, col. 2). If such confirmation is only routine, why is it that from the time Chatenoud et al. was published (Jan., 1994) until appellant filed this application (Dec. 1997), or nearly 4 years, appellant has not be able to disclose anything more particular with respect to human treatment in the specification than he did when he published Chatenoud et al.? The instant disclosure of an invention, particularly claiming treatment of humans, shows no

more development of the art of treating of humans than did Chatenoud et al., published nearly four years previously. The instant disclosure, in essence, merely expresses the same wish that Chatenoud et al. expressed. Nothing in particular is disclosed regarding treatment of humans, but for suggesting the use of any conventional carrier, any conventional route of administration, and a dose range extrapolated from Chatenoud et al. These features can be arrived at by anyone of acquaintance with the art by merely sitting at a word processor, rather than by conducting further experimentation that would reduce the invention to real world practice.

Appellant has urged (Brief page 8) that the examiner is legally erroneous because there is no objective evidence of record that one skilled in the art would have to undertake anything more than the kind and amount of experimentation that is endemic to the art. The examiner considers that the record per se presents the objective evidence. As noted in the above paragraph, the of record reference of Chatenoud et al. was published in Jan., 1994 and the instant application was filed nearly 4, years later, in Dec., 1997. If the amount of experimentation required to reduce humans to actual practice is routine, why then was the appellant able to offer nothing more than a handful of conventional directions or extrapolations from Chatenoud et al. specifically directed to treatment of humans, which is obviously the most desirable of all possible embodiments? If efficacy for humans needed to be confirmed at the time

Chatenoud et al. published, then it would still need to be confirmed, because the instant disclosure adds little more particularly directed to treatment of humans.

Finally, regarding the 112 enablement rejection, the examiner notes that appellant has urged that animal experimentation is sufficient and human exemplification is not required, in order to establish enablement. Appellant cites In re Brana 34 USPQ 2d 1437 to support his position. The examiner notes, however, that the fact situation in Brana involved only a 112 enablement rejection, on the basis that animal experiments cannot enable human treatment; in that case there was no 103 reference published by the appellants showing essentially the same animal experiments shown in the specification. Instantly appellant has published the 103 reference of Chatenoud et al. showing animal experiments. Given the breadth of the instant claims, with respect to the types of anti-CD3 active compounds that may be embodied, and given the paucity of information in the specification, beyond what Chatenoud et al. taught, that is specifically directed to treatment of humans; the examiner considers that appellant must jump through a higher hoop to establish enablement than did Brana. The information published by appellant in Chatenoud et al. was already committed to the public. The examiner cannot determine what more the instant disclosure, as compared to that of Chatenoud et al., conveys to the public for the treatment of humans, except for a few statements of a general and conventional nature. In light of this fact, it is considered that the law requires that disclosure in an application must inform those skilled in the art how to use applicant's alleged

discovery, not how to find out how to use it for themselves. In re Gardner, Rose and Wiley 166 USPQ 138. Since the instant appellant has disclosed nothing of significance for human treatment, beyond what Chatenoud et al. disclosed, the examiner deems appellant unworthy of the right to exclude others as a quid pro quo reward for having conveyed so little to the public.

Regarding appellant's arguments concerning obviousness over Chatenoud et al., the examiner finds these to be confusing and missrepresentative of the reference. Appellant urges (page 9, second paragraph – page 10, first full paragraph) that Chatenoud et al. did not teach treatment of mice with overt/established/full-blown diabetes. As noted in the above statement of the rejection, the examiner finds that, in fact, mice with overt disease were treated.

Appellant argues that Chatenoud et al. used anti-CD3 antibodies and not F(ab')2 fragments thereof (paragraph spanning pages 9-10 and second full paragraph of page 10). The examiner cannot determine whether or not recitation of "anti-CD3" in the reference referred to the whole antibody, or was merely a short hand notation for its fragment. In any event, production of fragments is taught (page 123, col. 2). Furthermore, even if Chatenoud et al. used the whole anti-CD3 antibody, the use of such would clearly be encompassed by claims 1-2, 4, 6, 9-13 and 17-18. Note also, specification page 10, lines 18-23 teaching use of either the whole or the fragmented anti-CD3. Appellant is thus arguing a limitation, which is not a feature of any claims except 5 and 16.

Furthermore, with respect to claims 5 and 16, the examiner considers these obvious, since the use of whole antibodies or fragments thereof was art conventional. It appears that appellant did treat NOD mice having overt diabetes, with either whole anti-CD3 antibodies or F(ab')2 fragments thereof (specification, paragraph spanning pages 5-6). For some reason appellant only showed data for controls and for mice treated with the fragments (Table 1 at page 6). The specification thus fails to compare the efficacy of using an F(ab')2 fragment versus a whole antibody. If what Chatenoud et al. used to treat mice with overt diabetes was a whole anti-CD3 antibody, then the failure of the specification to compare effects of fragmented versus whole anti-CD3 antibodies precludes appellant from arguing, from any factual basis, that F(ab')2 fragments show any unexpected results over Chatenoud et al. claims 5 and 16 are thus maintained as obvious, and appellant has considered (Grouping of claims) that all claims stand or fall together.

Appellant has also urged (paragraph spanning Brief pages 10-11) that Chatenoud et al. did not teach that their experiments showed long-term/durable restoration of self-tolerance against autoantigens. Appellant urges therein that Chatenoud et al. could not have observed any efficacy beyond 50 days, due to death of CY treated mice. The examiner notes, however, that Chatenoud et al. teach a durable effect until 4 months, at which time the mice were sacrificed for histological studies (paragraph spanning pages 126-127). The examiner finds that the specification follows the effect of the treatment for 20 weeks. Taking 4

months as 18 weeks, the examiner finds that the instant disclosure teaches little more than the reference in terms of durability of the self-tolerizing treatment.

Finally, with respect to obviousness, the examiner notes arguments pertaining to the use of whole antibodies or of fragments and pertaining to the durability of the treatment were previously considered non-persuasive by the BPAI (Paper 24, Decision on appeal maintaining a rejection over Chatenoud et al. under 102). Appellant has urged (instant Brief last paragraph of page 8 – first paragraph of page 9). That the examiner is erroneous in asserting that changing the claim from a recitation of "mammal"" to "human" does not overcome what was found by the Board. The examiner considers this argument to be mere pleading since the Board considered that arguments pertaining to "durable" and 'transient" effects were not relevant to what is recited in the claimed invention and because the stated end result would be inherently achieved when conducting the same steps described by Chatenoud et al. Since appellant's amendment of claim 1, in response to the Board decision, has changed nothing regarding the steps that would be conducted, except for narrowing the scope of the subject upon which these steps would be conducted; the examiner considers it proper to carry through the findings of the BPAI regarding anticipation to obviousness.

As a concluding comment the examiner notes the statement of a 112-enablement rejection and of a 103 prior art rejection, has been made in a circumstance where the specification does not appear to add anything not taught

by the prior art. The examiner does not have sufficient evidence to determine which rejection is more appropriate, i.e., the art rejection or the enablement rejection. If the specification is enabling, so is the reference, and the claims may be unpatentable over the teachings of that reference. The examiner need not choose, based on the limited evidence, the rejection that is the more correct one, as the result is the same in either instance – the claims are unpatentable. It is thus proper for the examiner to make the superficially inconsistent art and enablement rejections, and place the burden on applicant to distinguish his or her specification from the prior art and to point out how the specification goes beyond and elaborates upon what is taught by the previously published reference. The examiner need not establish which of these two alternative rejections is correct, since the result would be the same no matter which is correct. Note In re Kravish 12 USPQ 257.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

D. A. Saunders:jmr
November 4, 2003

Conferees
Anthony Caputa
Christina Chan

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644

STEPHEN A BENT
FOLEY & LARDNER
3000 K STREET NW SUITE 500
PO BOX 25696
WASHINGTON, DC 20007-8696

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600